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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/527,666	08/01/2005	Christophe de Romeuf	065691-0387	7253

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EXAMINER	
CROWDER, CHUN	
ART UNIT	**PAPER NUMBER**
1644	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/05/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/527,666	DE ROMEUF ET AL.	
	Examiner	Art Unit	
	Chun Crowder	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04/05/2006 and 10/06/2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13 and 14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13 and 14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *08/09/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment, filed 04/05/2006, is acknowledged.

Claims 1-12 have been canceled.

Claims 13 and 14 have been added.

Claims 13 and 14 are pending.

2. Applicant's election with traverse of chronic myeloid leukemia, filed 10/06/2006, is acknowledged. The traversal is on the ground that the method of treating human cancer using anti-GM2 antibody taught by Nakamura et al. is targeting at ganglioside GM2 antigen that is strongly expressed on the surface of the cells in lung cancer; therefore, the prior art teachings are different from the claimed invention in that the instant invention is drawn to the treatment of pathologies from which the number of antigenic sites or the antigenic density is low.

This is not found persuasive because Nakamura et al. teach that the ganglioside GM2 is a major tumor differentiation antigen in human malignant melanomas and other tumors of neuroectodermal origin (see Introduction on pages 1035). Applicant has shown that the GM2 antigen is strongly expressed in human lung cancer cells; however, this does not indicate that the number of the GM2 antigen sites or the antigenic density in lung cancer cells are high, nor does this indicate the level of antigen sites or antigenic density in other types of cancers, e.g. melanomas and tumors of neuroectodermal origin. Further, even if GM2 antigen is strongly expressed in human lung cancer cells, applicant has not determined whether the antigenic sites or the antigenic density of the GM2 antigen is high in human lung cancer cells. Given that the claimed "the number of antigenic sites or the antigenic density is low" is indefinite (see discussion below); the claimed species of pathologies have no special technical feature that defined the contribution over the prior art of Nakamura et al. (Molecular Immunology 2000. 37:1035-1046). Thus, the finding of Lack of Unity of Invention has been maintained.

The requirement is still deemed proper and is therefore made FINAL.

Claims 13 and 14 are currently under consideration as they read on the elected species of a method of treating chronic myeloid leukemia.

3. This Office Action will be in response to applicant's arguments, filed 04/05/2006 and 10/06/2006.

The rejections of record can be found in the previous Office Action, mailed 12/05/2005.

The text of those Sections of Title 35 U.S.C. not included in this Action can be found in a prior Action.

4. Applicant's IDS, filed 08/09/2006, is acknowledged and has been considered.

5. Applicant's submission of the certified English translations (filed 05/11/2006) of the foreign priority documents FRANCE 02/11415, FRANCE 02/11416 and FRANCE 03/07066 is acknowledged.

However, the provisional application FRANCE 02/11415 and FRANCE 02/11416 upon which priority is claimed fail to provide adequate support under 35 U.S.C. 112 for the instant claims. Specifically, insufficient support was identified for the limitation of "chronic myeloid luekemias". Consequently, the claims have been accorded the foreign priority of the filing date of the FRANCE 03/07066, i.e. 06/12/2003.

Should applicant disagree with the Examiner's factual determination above, it is incumbent upon applicant to provide a showing that specifically supports the instant claim limitations.

6. Upon further consideration as well as applicant's amendments to the claims, the previous rejections under **35 U.S.C. 112, second paragraph and 35 U.S.C. 102(e)** have been withdrawn.

7. Upon consideration as well as applicant's amendment to the claims, the following **New Grounds of Rejection** have been set forth herein.

8. **This is a New Ground of Rejection.** Claims 13 and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 13 and 14 are indefinite in the recitation of "the number of antigenic sites or the antigenic density is low" because the phrase "the number of antigenic sites or the antigenic density is low" is a relative term which renders the claims indefinite. The term is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention.

B) Claims 13 and 14 are indefinite in the recitation of "optimized human or humanized monoclonal antibody" because the metes and bounds of the activities is not clear and ambiguous. For example, page 6 of the specification discloses that antibodies can be made in rat myeloma YB2/0 line; however, it is unclear what "optimized human or humanized monoclonal antibody" encompasses.

C) Applicant is reminded that any amendment must point to a basis in the specification so as not to add new matter. See MPEP 714.02 and 2163.06.

9. **This is a New Ground of Rejection.** The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 13 and 14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 13 and 14 are drawn to a method for treating pathologies e.g. chronic myeloid leukemia as elected species comprising administering an optimized human or humanized monoclonal antibody.

The instant claims encompass a method for treating pathologies by administering an optimized human or humanized monoclonal antibody without setting forth the antigen specificity for the claimed antibody.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification does not provide a sufficient enabling description of the claimed invention. The disclosure appears to disclose only in vitro ADCC effect of anti-CD20 antibody anti-HLA-DR antibody and anti-D monoclonal antibodies (see Examples on pages 19 of the instant specification). However, the specification does not appear to show any working examples the claimed method of treating pathologies, especially the elected chronic myeloid leukemia.

The state of art at the time the invention was made recognized that CD20 is a B cell surface antigen (Countouriotis et al. Stem Cells 2002, 20:215-229) and anti-CD20 antibody (e.g. Rituximab) has been used to treat diseases such as lymphomas (see pages 216-219 in particular); however, anti-CD20 antibody has not been shown to be used in the claimed method of treating chronic myeloid leukemia.

The current treatment options for chronic myeloid leukemia (Boccarani et al. Blood 2006. 108;6:1809-1820) include tyrosine kinase inhibitor, imatinib mesylate, recombinant IFN-α, low-dose arabinosyl cytosine (LDAC), allogeneic hematopoietic stem cell transplantation and do not include any disease specific antibodies (see Conclusions on pages 1816-1817, in particular).

Consequently, the experimentation left to those skilled in the art to determine which human or humanized antibody can be used in a method of treating pathologies such as chronic myeloid leukemia is unnecessarily, improperly, and extensive and undue.

In view of the lack of predictability of the art to which the invention pertains, working examples, the state of the art teachings, undue experimentation would be required to practice the claimed invention.

11. Claims 13 and 14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The following *written description* rejection is set forth herein.

Claims 13 and 14 recite "antigenic sites or the antigenic density" and claim 14 recites "rat myeloma lines" and "YB2/0 and its derivatives" as part of the invention.

There is insufficient written description in the specification as-filed of "antigenic sites or the antigenic density", "rat myeloma lines", and "YB2/0 and its derivatives" as recited in the instant claims.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. (See Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, especially page 1106 3rd column). A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. MPEP 2163 II.A.3a.ii.

The claims recite a genus "antigenic sites or the antigenic density", "rat myeloma lines" and "YB2/0 and its derivatives" as part of the invention without providing a physical structure or testable functional activity for the antigen and/or YB2/0 derivatives.

The genus of the "antigenic sites or the antigenic density", "rat myeloma lines" and "YB2/0 and its derivatives" are therefore extremely large. Applicant has disclosed CD20 antigen and YB2/0 cell (see Example 6 on pages 11-13). Thus Applicant has disclosed only a limited species of the antigen, rat myeloma lines and YB2/0 derivatives, namely CD20 and YB2/0 cell. The claimed "antigenic sites or the antigenic density", "rat myeloma lines" and "YB2/0 and its derivatives" lack a common structure essential for their function and the claims do not require any particular structure basis or testable functions be shared by the instant "antigenic sites or the antigenic density", "rat myeloma lines" and "YB2/0 and its derivatives".

It does not appear based upon the limited disclosure of CD20 and YB2/0 cell alone that Applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the limited number of species disclosed and the extensive variation permitted within the genus of "antigenic sites or the antigenic density", "rat myeloma lines" and "YB2/0 and its derivatives".

"Adequate written description requires a precise definition, such as by structure, formula, chemical name or physical properties, not a mere wish or plan for obtaining the claimed chemical invention." Regents of the University of California v. Eli Lilly and Co. 43 USPQ2d 1398 (Fed. Cir. 1997).

The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter of the claim. Id. 43 USPQ2d at 1406.

In the absence of disclosure of relevant, identifying characteristics of the "antigenic sites or the antigenic density", "rat myeloma lines" and "YB2/0 and its derivatives", there is insufficient written disclosure under 35 U.S.C. 112, first paragraph.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 1115).

12. **This is a New Ground of Rejection.** The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country. more than one year prior to the date of application for patent in the United States.

13. Claims 13 and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Ogawa (EP 1229125, published 07/08/2002) (see entire document).

Ogawa teaches that antibodies e.g. humanized antibodies, made in YB2/0 host cells, have a higher antibody-dependent cell-mediated cytotoxic activity (ADCC) and are useful as a pharmaceutical agents for treating diseases such as breast cancer (see entire document, particularly columns 3-5).

Given the referenced antibodies are made in the same host cells (YB/2/0) as the claimed antibodies, the claimed limitation of the glycan structures would be inherent properties of the antibodies taught by Ogawa.

Therefore, the reference teachings anticipate the claimed invention.

14. *Conclusion: no claim is allowed.*

15. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chun Crowder whose telephone number is 571-272-8142. The examiner can normally be reached on 8:30-5:00. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Chun Crowder, Ph.D.
Patent Examiner
December 19, 2006

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12/12/06